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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,144	03/29/2004	Emmanuel Cyrille Pascal Briend	674525-2011	3079
20/999 7590 07/01/2008 FROMMER LAWRENCE & HAUG 745 FIFTH AVENUE- 10TH FL. NEW YORK, NY 10151				
EXAMINER				
WANG, CHANG YU				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/812,144

Applicant(s)

BRIEND ET AL.

Examiner

Chang-Yu Wang

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 12, 14, 37 and 66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-5, 16, 17, 30, 33, 36, 42, 47, 49-51, 53-57, 60, 61, 65, 100 and 101 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-848)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continuation of Disposition of Claims: Claims pending in the application are 1,3-5,12,14,16,17,30,33,36,37,42,47,49-51,53-57,60,61,65,66,100 and 101.

DETAILED ACTION
RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed 10/31/07 is acknowledged. Claims 2, 6-11, 13, 15, 18-29, 31-32, 34-35, 38-41, 43-46, 48, 52 and 67-99 are cancelled. Claim 101 is amended. Claims 1, 3-5, 12, 14, 16, 17, 30, 33, 36, 37, 42, 47, 49-51, 53-57, 60, 61, 65, 66, 100 and 101 are pending in this application. Claims 12, 14, 37 and 66 are withdrawn with traverse (the response filed 9/18/2006) from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.
3. Claims 1, 3-5, 16, 17, 30, 33, 36, 42, 47, 49-51, 53-57, 60, 61, 65, 100 and 101 are under examination in this office action.
4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.

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5. Applicant's arguments filed on 10/31/07 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

6. The rejection of claim 101 under 35 U.S.C. 112, second paragraph, for being indefinite is withdrawn in response to Applicant's amendment to the claim by reciting a specific structure for formula I.

The rejection of claims 1, 3-5, 16, 17, 30, 33, 36, 42, 47, 49-51, 53-57, 60, 61, 65, 100 and 101 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No.10/899422, claims 17-20 of copending Application No.11/058066, claims 1-20 of copending Application No. 11/178724 is withdrawn because these copending applications have been abandoned.

Claim Rejections/Objections Maintained

In view of the amendment filed on 10/31/07, the following rejections are maintained.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5, 16, 17, 30, 33, 36, 42, 47, 49-51, 53-57, 60, 61, 65, 100 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting the Notch signaling induced by Delta-1 (a Notch ligand) in C2C12

cells and Jurkat-N2 cells with MW167, and enabling for inhibiting the production of notch-mediated cytokines by measuring decreased IL-10 and increased IL-5 in human CD4⁺ T cells isolated from peripheral blood in vitro, does not reasonably provide enablement for a method for decreasing regulatory CD4⁺ T cell activity by a structurally undefined inhibitor of presenilin or of presenilin-dependent gamma-secretase as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The rejection is maintained for the reasons made of record in the office action mailed 8/20/07, and as follows.

At p. 6 of the response, Applicant argues that instant claims are enabled because the specification describes inhibitors that can be used in the claimed method and the specification also provides guidance and working examples as to how to identify the inhibitors. Applicant further argues that different types of gamma-secretase inhibitors were known in the art as shown in Doefer and Strooper. Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicants' assertion, the specification fails to provide sufficient guidance as to enable one of skill in the art to practice the full scope of the invention because the inhibitors are not limited to the ones disclosed by Doefer and Strooper. Although several inhibitors of presenilin or presenilin-dependent gamma secretase are known in the art, the recitation of "inhibitors of presenilin or presenilin-dependent gamma secretase" encompasses almost any agent, including those yet to be discovered. In addition, Applicants fail to teach what common structure/characteristics

are required for the agent that down-regulates the Notch signaling as recited in claim 5. Therefore, a skilled artisan would not know how to make the components required to practice the currently claimed method because the structural and functional correlation between the claimed agent and the claimed invention is undefined, and thus unknown. Furthermore, Applicants fail to teach what specific antigen or antigen determinants as recited in claims 16-17 are and thus can be used in the claimed methods. Although Notch has been shown to be involved in tumorigenesis and immune tolerance, without guidance of specific antigens or antigen determinants, a skilled artisan cannot contemplate how to use the claimed invention since no define antigen or antigen determinant is provided.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity is unpredictable and the experimentation left to those skilled in the art is extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed invention as currently claimed without further undue experimentation. Accordingly, the rejection of claims 1, 3-5, 16, 17, 30, 33, 36, 42, 47, 49-51, 53-57, 60, 61, 65, 100 under 35 U.S.C. §112, first paragraph, because the specification does not enable the invention in scope commensurate with the claims is maintained.

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8. Claims 1, 3-5, 16, 17, 30, 33, 36, 42, 47, 49-51, 53-57, 60, 61, 65, 100 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is maintained for the reasons made of record in the office action mailed 8/20/07, and as follows.

At p. 6-7 of the response, Applicant argues that instant claims meet the written description requirement because the specification provides support the claimed inhibitors of presenilin or presenilin-dependent gamma secretase and several inhibitors are known in the art. Applicant's arguments have been fully considered but they are not persuasive.

In response, although several inhibitors are known in the art and the specification describes MK167 with formula I, Applicant fails to demonstrate Applicant's possession of the genus of inhibitors that can be used in the claimed method because the claims are not limited to the MK167 or inhibitors disclosed in the specification. Applicant also fails to demonstrate the genus of agents that can down-regulates the Notch signaling as recited in claim 5. The specification fails to teach what common structures or amino acid sequences are required for the claimed genus of inhibitors. Since the structural and functional relationship of the claimed inhibitors or agents is unknown, a skilled artisan cannot envision the functional correlation between the claimed agents/inhibitors and the claimed method. Thus, the specification fails to reasonably demonstrate Applicant's

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possession of such broad genus of inhibitors/agents that can be used in the claimed method. Note that

A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004).

Obviousness-Type Non-Statutory Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5, 16, 17, 30, 33, 36, 42, 47, 49-51, 53-57, 60, 61, 65, 100 and 101 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-38 of copending Application No. 10/765727, claims 16, 20, 21, 24-32, 61-70, 72 of copending Application No. 10/846989, claims 28-61, 86, 100-119 of copending Application No. 10/845834, claims 24-33 of copending Application No. 10/958784, claims 1-7 of copending Application No. 11/071796, claims 65, 68-73 of copending Application No. 11/232404, claims 4-6 of

copending Application No. 11/231494, and claims 20-41 of copending Application No. 11/495015. The rejection is maintained for the reasons made of record in the office action mailed 8/20/07, and as follows.

At p. 7 of the response, Applicant requests that the rejections be held in abeyance until conflicting claims are patented. Applicants' argument has been fully considered but it is not persuasive. The rejection of claims under obviousness double patenting for being unpatentable over the claims of copending Application Nos. 10/765727, 10/846989, 10/845834, 10/958784, 11/071796, 11/232404, 11/231494, and 11/495015 is maintained of record until a terminal disclaimer is filed.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3-5, 30, 33, 42, 47, 49-51, 53-57, 60, 61, 100 stand rejected under 35 U.S.C. 102 (b) as being anticipated by Doerfler et al. (PNAS, 2001. Jul 31. 98: 9312-9317). The rejection is maintained for the reasons made of record in the office action mailed 8/20/07, and as follows.

At p. 8 of the response, Applicant argues that Doerfler does not teach the claimed method because Doerfler does not teach that the inhibitor can induce a decrease of CD4+ regulatory T cell activity and Hoyne only teaches the effects of Notch signaling on

naïve T cells and their differentiation into regulatory T cells not the effects on regulatory T cell activity. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, Doerfler does teach the claimed method of decreasing regulatory CD4⁺ T cells activity by an inhibitor of presenilin-dependent gamma-secretase as recited in instant claims 1, 3 and 4 because decreasing CD4⁺ T cell activity is an inherent result of administration of an inhibitor of presenilin-dependent gamma-secretase (i.e. compounds 1-3, which bind to presenilin-1 and -2) in thymic organ cultures (see p. 9313, 2nd col., 2nd paragraph; p. 9314, 2nd col., 2nd paragraph to p. 9315, 1st col., in particular). The inactivation of Notch-1 in thymic organ cultures by presenilin- γ -secretase inhibitors as taught by Doerfler would inherently decrease CD4⁺ regulatory T cell activity because the thymic organ cultures encompass different subsets of T cells including CD4⁺ regulatory T cells. Thus, the decreased activity of CD4⁺ regulatory T cells (claims 1, 30, 33) and modulation of cytokine expression in regulatory CD4⁺ T cells are inherent results of inhibiting Notch-1 signaling by an inhibitor of presenilin (PS-1 and PS-2) or presenilin-gamma secretase in the thymic organ cultures.

In addition, as previously made of record, Hoyne et al. teach that the changes of different subsets of T cells and the changes of cytokines are natural processes of the immune response to an inhibitor of the Notch signaling pathway because regulatory T cells include CD4⁺CD25⁺ T regulatory cells, IL-1-secreting Tr1 cells and Th3 cells, and different cytokine expression can be mediated by these different T cells. Thus, the regulatory T cell activity includes modulating the expression of different cytokines and

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modulating different subsets of T cells maturation. The changes of subsets of CD4⁺ T cells such as decreasing CD4⁺ regulatory T cell activity and decreasing or increase cytokines as recited in instant claims 1, 30, 33, 42, 47, 49-51, 53-57, 60, 61 are inherent results in response to an inhibitor of the Notch signaling pathway in vitro or in the immune system in vivo because the responses of T cells and cytokines as well as the properties/features of different T cells and cytokines are an natural immune response to administration of an inhibitor of Notch IC protease activity.

Furthermore, as previously made of record, no active steps for subsets of CD4⁺ T cells are recited in claims 30, 33 and no active step for cytokines are recited in claims 42, 47, 49-51, 53-57, 60, 61. The recitations of the changes of the subsets of CD4⁺ T cells and cytokines in these claims are descriptive mechanisms of an immune response in response to an antigen or a combination of antigen with an inhibitor of the Notch signaling pathway in vitro or in the immune system in vivo. Independent claims 1 and 42 only recite "exposing a regulatory CD4⁺ T cell to an inhibitor of presenilin or of presenilin-dependent gamma-secretase, which is taught by Doerfler. Thus, Doerfler teaches the claimed method because Doerfler teaches administration of an inhibitor of presenilin-dependent gamma-secretase to thymic organ cultures and the responses such as decreasing CD4⁺ regulatory cell activity and the changes of the expression of cytokines in thymic organ cultures would inherently respond to the inhibitors. Accordingly, the rejection of claims 1, 3-5, 30, 33, 42, 47, 49-51, 53-57, 60, 61, 100 as being anticipated by Doerfler et al. is maintained.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-5, 16, 17, 30, 33, 36, 42, 47, 49-51, 53-57, 60, 61, 65, 100 and 101 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Doerfler et al. (PNAS, 2001. Jul 31. 98: 9312-9317) in view of Strooper et al. (Nature. 1999. 398:518-522 as in IDS, cited in the previous office action) and Lamb et al. (WO01/35990, published May 25, 2001, as in IDS). The rejection is based on what is enabled in the claims. The rejection is maintained for the reasons made of record in the office action mailed 8/20/07, and as follows.

At p. 8-9 of the response, Applicant argues that the cited references do not render the claimed invention obvious because Doerfler does not teach a method of decreasing regulatory CD4+ T cell activity and neither Strooper nor Lamb remedies the

deficiencies in Doerfler. Applicant's arguments have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In contrast, Doerfler does teach the claimed method of decreasing regulatory CD4+ T cell activity by an inhibitor of presenilin or presenilin-dependent gamma-secretase as set forth above at paragraph 10. Although Doerfler fails to teach that the presenilin-dependent γ -secretase inhibitor is a MW167 as recited in instant claim 101, Strooper teaches that several γ -secretase inhibitors, including MW167, are able to inhibit the processing of Notch1 to release Notch IC as recited in instant claims 1, 42, and 101 (see p. 520, 1st col., 1st paragraph to 2nd col., 2nd paragraph). It would have been obvious to a skilled artisan at the time the instant invention was made to use an inhibitor of Notch IC protease activity, such as MW 167, in the method of Doerfler to decrease regulatory T cells and to decrease the expression of IL-10 or IL-4 and to increase the production of IL-5 because γ -secretase inhibitors, including MW167, are able to inhibit the processing of Notch1 to release Notch IC as the inhibitors of presenilin or presenilin-dependent gamma-secretase disclosed by Doerfler.

In addition, although Doerfler fails to teach an antigen as recited in instant claims 16 and 17 and also fails to teach administration of an inhibitor in vivo as recited in

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instant claims 36 and 65, Lamb (WO01/35990) teaches methods of immunotherapy and cancer therapy by blocking the Notch signaling pathway with an inhibitors and an antigen in vivo as in claims 1 and 16-17 (see p.21-23; p.30-31). Lamb teaches treatment of cancer by vaccination or reintroduction of T cells, antigen presenting cells or tumor cells isolated from patients and treatment with an agent that down-regulates the expression of Notch and Notch ligands such as Serrate/Delta or decreases the interaction between Notch and Notch ligand to block the Notch signaling pathway and thereby enhance tumor-antigen recognition as in claims 16-17, 36 and 65 (see p. 8-9; 21-23; 30-31). The teachings of Lamb (WO'990) provide a motivation to one of skill in the art to enhance the cellular immunity that regulates tumor or infection as in claims 16-17, 36 and 65 by inhibiting the Notch signaling pathway using an inhibitor of the Notch signaling pathway because activation of the Notch signaling pathway reduces T cell activation in allergy and immune tolerance, and increases regulatory T cells. The teachings of Lamb (WO'990) also provide a motivation and an expectation of success in using a combination of a tumor antigen with an inhibitor of presenilin or presenilin- γ -secretase to block the Notch signaling pathway that is involved in tumorigenesis and enhance tumor recognition. Thus, the applied references render the claimed invention obvious because abnormal activation of the Notch signaling pathway is involved in tumorigenesis and blocking the Notch signaling with a combination of a tumor antigen with an inhibitor of presenilin or presenilin- γ -secretase would inhibit tumorigenesis.

In addition, it would also have been obvious to a skilled artisan at the time the instant invention was made to use an inhibitor of Notch IC protease activity, such as

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MW 167, or in combination with a tumor or a pathogen antigen or antigen determinant, to decrease regulatory T cells, to decrease the expression of IL-10 or IL-4 and to increase the production of IL-5, and thereby to enhance the immunity against tumor and infection. The person of ordinary skill in the art would have been motivated to do so with an expectation of success because the activation of the Notch signaling pathway is involved in tumorigenesis and immune tolerance, the abnormal activation of the Notch signaling pathway is involved in tumorigenesis and blocking the Notch signaling using an inhibitor of Notch IC protease activity, MW167, would inhibit tumorigenesis.

Conclusion

12. NO CLAIM IS ALLOWED.

13. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/

Chang-Yu Wang, Ph.D.

June 16, 2008

/Christine J Saoud/

Primary Examiner, Art Unit 1647